Remarks

I. Preliminary Amendment

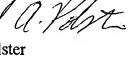
Applicants have amended the first page of the specification by adding a sentence to reflect priority claims. Pages 8 and 9 were unclear, and page 83 was missing from the parent case 09/141,547, filed Aug. 28, 1998, although they appeared in priority document U.S. application Serial No. 08/824,626 filed March 27, 1997, and are submitted in Appendix 1.

Applicants have canceled the original claims and have added a new claim in this preliminary amendment. Support for the new claim can be found on page 1, line 28, pages 4-9, and page 23, line 34.

The Applicants do not believe that any additional fees are due; however, the Office has the authority to charge the Applicants' Deposit Account for any fees that are presently due, or any fees that will become due. Please charge any appropriate fees to Deposit Account No. 19-1025.

If the Examiner believes a telephonic interview with Applicant's representative would aid in the prosecution of this application, he or she is cordially invited to contact Applicant's representative at the below listed number.

Respectfully submitted,



Rachel A. Polster
Agent for Applicants
Reg. No. 47,004
314-274-7354 (St. Louis)

PHARMACIA CORPORATION
Corporate Patent Law Department
P.O. Box 1027
Chesterfield, Missouri 63006

wherein Y^2 is selected from the group consisting of H, alkyl; cycloalkyl; bicycloalkyl; aryl; monocyclic heterocycles; alkyl optionally substituted with aryl which can also be optionally substituted with one or more substituent selected from halo, haloalkyl, alkyl, nitro, hydroxy, alkoxy, aryloxy, aryl, or fused aryl; aryl optionally substituted with one or more substituent selected from halo, haloalkyl, hydroxy, alkoxy, aryloxy, aryl, fused aryl, nitro, methylenedioxy, ethylenedioxy, or alkyl; alkynyl; alkenyl; $-S-R^9$ and $-O-R^9$ wherein R^9 is selected from the group consisting of H; alkyl; aralkyl; aryl; alkenyl; and alkynyl; or R^9 taken together with R^7 forms a 4-12 membered mononitrogen containing sulfur or oxygen containing heterocyclic ring; and

R^5 and R^7 are as defined above;

or Y^2 (when Y^2 is carbon) taken together with R^7 forms a 4-12 membered mononitrogen containing ring optionally substituted with alkyl, aryl or hydroxy;

Z^1, Z^2, Z^4 and Z^5 are independently selected from the group consisting of H; alkyl; hydroxy; alkoxy; aryloxy; aralkoxy; halogen; haloalkyl; haloalkoxy; nitro; amino; aminoalkyl; alkylamino; dialkylamino; cyano; alkylthio; alkylsulfonyl; carboxyl derivatives; acetamide; aryl; fused aryl; cycloalkyl; thio; monocyclic heterocycles; fused monocyclic heterocycles; and A, wherein A is defined above;

R^{5O} is selected from the group consisting of H and alkyl;

R^1 is selected from the group consisting of H, alkyl, alkenyl, alkynyl, aryl and aryl, optionally substituted with one or more substituent selected from the group consisting of halogen, haloalkyl, hydroxy, alkoxy, aryloxy, aralkoxy, amino, aminoalkyl, carboxyl derivatives, cyano and nitro;

t is an integer 0, 1 or 2;

R is X-R^3 wherein X is selected from the group consisting of O, S and NR^4, wherein R^3 and R^4 are independently selected from the group consisting of hydrogen; alkyl; alkenyl; alkynyl; haloalkyl; aryl; arylalkyl; sugars; steroids and in the case of the free acid, all pharmaceutically acceptable salts thereof; and

Y^3 and Z^3 are independently selected from the group consisting of H, alkyl, aryl, cycloalkyl and aralkyl.

It is another object of the invention to provide pharmaceutical compositions comprising compounds of the Formula I. Such compounds and compositions are useful in selectively inhibiting or antagonizing the $\alpha_v\beta_3$ integrin and therefore in another embodiment the present invention relates to a method of selectively inhibiting or antagonizing the $\alpha_v\beta_3$ integrin. The invention further involves treating or inhibiting pathological conditions associated therewith such as osteoporosis, humoral hypercalcemia of malignancy, Paget's disease, tumor metastasis, solid tumor growth (neoplasia), angiogenesis, including tumor angiogenesis, retinopathy including diabetic retinopathy, arthritis, including rheumatoid arthritis, periodontal disease, psoriasis, smooth muscle cell migration and restenosis in a mammal in need of such

alkoxy, aryloxy, aryl, or fused aryl; aryl optionally substituted with one or more substituent selected from halo, haloalkyl, hydroxy, alkoxy, aryloxy, aryl, fused aryl, nitro, methylenedioxy, ethylenedioxy, or alkyl; alkynyl; alkenyl; $-S-R^9$ and $-O-R^9$ wherein R^9 is selected from the group consisting of H; alkyl; aralkyl; aryl; alkenyl; and alkynyl; or R^9 taken together with R^7 forms a 4-12 membered mononitrogen containing sulfur or oxygen containing heterocyclic ring; and

R^5 and R^7 are as defined above;

or Y^2 (when Y^2 is carbon) taken together with R^7 forms a 4-12 membered mononitrogen containing ring optionally substituted with alkyl, aryl or hydroxy;

Z^1, Z^2, Z^4 and Z^5 are independently selected from the group consisting of H; alkyl; hydroxy; alkoxy; aryloxy; arylalkoxy; halogen; haloalkyl; haloalkoxy; nitro; amino; aminoalkyl; alkylamino; dialkylamino; cyano; alkylthio; alkylsulfonyl; carboxyl derivatives; acetamide; aryl; fused aryl; cycloalkyl; thio; monocyclic heterocycles; fused monocyclic heterocycles; and A, wherein A is defined above;

R^{50} is selected from the group consisting of H and alkyl;

R^1 is selected from the group consisting of H, alkyl, alkenyl, alkynyl, aryl and aryl, optionally substituted with one or more substituent selected from the groupo consisting of halogen, haloalkyl,